ORIGINAL RESEARCH PAPER

Volume-7 | Issue-1 | January-2018 | PRINT ISSN No 2277 - 8179

INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

COMPARING THE EFFECTS OF IMIPRAMINE, SERTRALINE AND ESCITALOPRAM ON LIPID PROFILE IN PATIENTS WITH MAJOR DEPRESSION: AN OBSERVATIONAL STUDY

Medical Science

Dr. Vandana Goyal Professor, Department of Pharmacology, JLN Medical College Ajmer, Rajasthan (India)

Preeti Sharma Statistical Officer, JLN Medical College Ajmer, Rajasthan (India)

Arun Kumar Sharma* Senior Demonstrator (Ph.D. Scholar), Department of Pharmacology, JLN Medical College Ajmer, Rajasthan (India) *Corresponding Author

ABSTRACT

Depression is a state of low mood and aversion to activity that can affect a person's thoughts, behaviour, feelings and sense of well-being. It accounts 4.3% of total disability-adjusted life years. If current trends continue, it will become the leading cause of disease burden by the year 2030. Several previous studies have reported an association between low cholesterol level and major depressive disorder. Some studies demonstrated the relationship between dyslipidaemia and various psychiatric disorders. This open lable, prospective and observational study was conducted to evaluate the lipid profile of patient with major depressive disorder. A total of 810 newly diagnosed major depressive patients as per DSM-V criteria were divided into three groups i.e. group I, II & III consisting of 270 patients in each group were enrolled. Imipramine, sertraline and escitalopram as per schedule dose were given in these groups respectively. After completion of treatment, there was a significant increase in mean value of total cholesterol, triglycerides, HDL & LDL in all the three groups but these increase were within recommended range.

Conclusion: We conclude that a significant increase in mean value of total cholesterol, triglycerides, HDL & LDL in all the three groups but this increase were within recommended range. Evaluation of lipid profile in such type patient is essential to avoid any cardiovascular risk.

KEYWORDS

Depression, Lipid profile, Imipramine, Sertraline and Escitalopram

Major Depressive Disorder commonly called major depression, unipolar depression or clinical depression. It is also known simply as depression and is characterized by one or more Major Depressive Episodes [1]. In terms of public health significance, depression is the third leading cause of global disease burden, accounting for 4.3% of total disability-adjusted life years. If current trends continue, it will become the leading cause of disease burden by the year 2030 [2,3].

Cholesterol is an important component of biological membranes. It affects the fluidity of cell membrane and membrane permeability. It is also required for the correct functioning of neurotransmission in the central nervous system [4, 5]. Several previous studies have reported an association between low cholesterol level and major depressive disorder [6-9]. Some studies demonstrated the relationship between dyslipidaemia and various psychiatric disorders [10-12].

The aim of this study is to evaluate the lipid profile of patient with major depressive disorder. In Indian scenario, there is very little literature available in which conventional drugs were compared with newer ones especially on lipid profile of patient with major depressive disorder, therefore we undertook this study.

Methodology: This open label, prospective and comparative observational study was conducted after obtaining the approval from the institutional ethics committee & approval from Rajasthan University of Health Sciences, Jaipur (RUHS).

Source of data: Patients of depressive disorder visiting OPD (Out Patient Department) of psychiatric department of JLN Medical College & Associate group of Hospitals, Ajmer (Rajasthan).

Inclusion/exclusion criteria:

Patients of either sex aged between 18-65 years suffering from mild to moderate depressive disorder as per Beck Depression Inventory Scale score, who gave their consent for this research were enrolled since August 2016. Patients being treated with more than one antidepressant, having psychotic depression, bipolar disorder, schizophrenia or anxiety disorders, current suicidal ideation, serious decompensated medical conditions like congestive cardiac failure, renal failure, and Hepatic failure, or any other abnormalities, pregnant and lactating and any other patients who do not fulfil the inclusion criteria were excluded.

Study subjects (total- 810) fulfilling the inclusion/exclusion criteria were randomly assigned into three groups of 270 patients in each group as follows:

Group I: Study subjects were treated with imipramine orally in a dose of 75 mg BD.

Group II: Study subjects were treated with sertraline orally in a dose of 150 mg daily (i.e. 50 mg in morning and 100 mg in night)

Group III: Study subjects were treated with escitalopram orally in a dose of 10 mg BD.

Biochemical analysis of serum cholesterol was done by standard method [13].

Clinical assessment details during enrolment visit as well as follow up at 4 weeks, 8 weeks, and 12 weeks were recorded in study performa and analysed. Data were analysed as per appropriate statistical method.

Results: A total of 187 patients in group I whereas 228 and 237 patients in group II & group III respectively completed this study. Significant intergroup differences in total Cholesterol (mg/dl) were observed at baseline and all the time intervals. At baseline and 4 weeks intervals, there is significant difference in total Cholesterol among all groups. At 8 week and 12 week intervals, significant intergroup group differences for the pair I vs III and II vs III were observed. However, the difference between Groups I and II was not significant at 8 and 12 weeks follow up (Table-1a).

Table-1(b) shows all the three groups a significant increase in mean values was observed after the completion of treatment ($p<0.001$).

From table- 2(a), at baseline and 12 weeks follow up, intergroup difference of mean values were not significant, however, at 4 and 8 weeks intergroup differences were significant. At 4 weeks and 12 weeks follow up intervals, mean value in group III was significantly greater than mean value in Group II and Group I. Similarly, for the same intervals mean values in group II is significantly greater than mean value in Group I.

After completion of treatment, all the three groups showed a significant increase in mean values ($p<0.001$). (Table-2b)

At baseline, there was no significant intergroup difference ($p=0.979$), and other three groups show significant mean difference among groups. At 4 week interval mean HDL value of Group III is statistically less than mean HDL value of Groups I and II. On the other hand, at week 4 week and 8 week intervals, mean value of Group III is significantly greater than Group I and II (Table 3a).

A significant increase in mean values was observed for all the three groups ($p<0.001$). The extent of increase was maximum in Group III (Table 3b).

As shown in table 4 (a), at baseline, mean values were minimum in Group III followed by Group I and Group III respectively, and statistically significant intergroup difference ($p<0.001$) was observed among all groups. At 4 weeks, mean value was maximum in Group II followed by Group I and then Group III and intergroup difference as well as all the three between group differences were significant statistically ($p<0.05$). At 8 and 12 weeks, Group I had maximum mean value followed by Group II, and then by Group III. However, at 8 and 12 weeks significant difference observed for only two pairs namely I vs III and II vs III, as p value observed for these pairs are less than 0.05.

After completion of treatment (at 12 weeks), all the three groups showed a significant increase ($p<0.001$) in mean value of LDL (mg/dl).The mean change was maximum in Group I and minimum in Group III (Table 4b).

These findings were consistent with study done by Divyashree et al. 2014, Esmaeil Shahsavand Ananloo et al. 2013 and Murat kesim et al. 2011 [14-16].

Discussion:

Cholesterol is an important component of biological membranes. It affects the fluidity of cell membrane and membrane permeability. It is also required for the correct functioning of neurotransmission in the central nervous system [4,5]. Several previous studies have reported an association between low cholesterol level and major depressive disorder [6-9]. A lot of studies have been performed to establish a relationship between cholesterol levels and depression. Majority of the studies have concluded that low cholesterol levels are associated with depression and suicide [17-18], whereas few studies have denied any relationship between the two. However exact pathophysiological mechanism linking cholesterol and depression is unclear and still debatable. Many studies suggested the relationship between lipid metabolism and serotonin function. Various hypotheses are proposed e.g. Papakostas et al. (2004) suggest that low serum cholesterol levels are associated with decreased serotonergic function [19]. It is also postulated that low serum cholesterol concentration alters the metabolism of serotonin that leads to depression and poor control of aggressive impulses, resulting in an increased risk of suicides [20].

Hawton et al (1993) hypothesized that lower plasma concentration of cholesterol may lead to lower cholesterol concentration in brain which in turn reduce serotonergic neuronal activity. Serotonergic activity is reduced in two distinct ways i.e. Increase in serotonin reuptake and decrease in number and function of serotonin receptors [21]. Penttinen J. (1995) suggested the role of interlukin-2 which can cause decrease in cholesterol and depression [22]. Tearo et al (1997) found a positive relationship between serum cholesterol and serotonin receptor function [23]. Lower serum high-density lipoprotein cholesterol (HDL-C) levels are probably induced by the immune/inflammatory response and there is an impairment of reverse cholesterol transport from the body tissues to the liver in cases of depression [24].

Various studies have shown that patients with major depression have low HDL-C concentrations and higher ratios of (TC/HDL-C) and (LDL-C/ HDL-C) [11, 24, 25]. It is also suggested that low TC [26], adiposity and high waist to hip ratio are associated with MD and suicidal behaviors [27].

Partonen et al (1999) investigated 30,000 participants of the Finnish community and found that low serum cholesterol levels were associated with depressed mood and a heightened risk of hospitalization for depression [28]. Rafter D (2001) found that patients with low cholesterol scored significantly higher on the Hamilton Rating Scale for Depression [29]. Troisi (2011) also confirmed the finding of low cholesterol in the patients of mood disorder [30]. Maes et al. (1997) found that lower serum HDL-C levels are a marker for major depression and suicidal behavior in depressed men [24]. Few investigators have also reported high levels of TC, LDL and triglycerides in depressive patients [31-32].

In several studies, it is also seen that various antidepressants and mood stabilizers, doxepin, imipramine, paroxetine and even following treatment with electroconvulsive therapy results in an increase in serum cholesterol levels [33-37]. However, few studies have also suggested that antidepressant drugs do not cause a rise in the cholesterol levels [38-39].

Few investigators have noted the association between TCAs and weight gain as well as association between SSRIs with abdominal obesity and hypercholesterolemia [40-43]. It has been suggested that activation of sterol regulatory element-binding protein (SREBP) may be important in understanding the metabolic side effects of psychiatric drugs. Imipramine and fluoxetine also activate SREBP system. It was also noted that downstream genes that were involved in the biosynthesis of cholesterol and fatty acid were upregulated by Imipramine and fluoxetine but to a different extent [44].

Lautt WW et al. (2010), Patarrao RS (2008) and Sadri P et al. (2006) hypothesised the role of hepatic insulin-sensitizing substance (HISS) [45-47]. Murat Kesim et al. (2011) noted that sertaline treatment may cause hypertryglyceridemia because of inhibition of conversion of triglycerides to VLDL in liver [16].

Based on our results and available literature, patients treated with imipramine, sertraline and escitalopram need to be followed up for lipid profile to avoid any risk for cardiovascular disease in depressive patients. Further studies are needed to evaluate the effects of long-term use of imipramine, sertraline and escitalopram on lipid profile.

Conclusion:

We conclude that a significant increase in mean value of total cholesterol, triglycerides, HDL & LDL in all the three groups but this increase were within recommended range. Evaluation of lipid profile in such type patient is essential to avoid any cardiovascular risk. As LDL Cholesterol was maximum increased in group I & minimum increased in group III, therefore we found escitalopram is safer than imipramine and sertraline. Further studies are needed to evaluate the effects of long-term use of imipramine, sertraline and escitalopram on lipid profile.

Table 1(a): Inter and between group comparison of Total Cholesterol (mg/dl)

Visits	Group I (n=270)			Group II (n=270)			Group III (n=270)			Statistical significance (ANOVA)* Between Group comparison (Tukey HSD test 'p' value)				
	No.	Mean	SD	No.	Mean	SD	No.	Mean	SD	F	'p'	I vs II	I vs III	II vs III
Baseline	270	138.00	7.26	270	140.86	7.52	270	132.98	6.25	86.76	<0.001	.000	0.000	0.000
At 4 wks	246	153.55	8.18	251	156.39	8.16	257	145.13	6.95	144.27	.000	.000	0.000	0.000
At 8 wks	207	165.79	8.81	234	165.23	8.77	244	151.26	7.22	233.28	.000	.758	0.000	0.000
At12wks	187	169.63	8.94	228	168.60	8.79	237	154.10	7.21	246.58	.000	.417	0.000	0.000

Table 1(b): Within Group evaluation of Change among patients completing 12 weeks of treatment

Group	No. of patients completing 12 wks treatment	At Baseline		At 12 weeks		Statistical Significance (Paired 't'-test)	
		Mean	SD	Mean	SD	't'	'p'
I	187	138.41	7.39	169.63	8.94	229.89	<0.001
II	228	140.80	7.65	168.60	8.79	207.45	<0.001
III	237	133.07	6.23	154.10	7.21	240.62	<0.001

Table 2 (a): Inter and between group comparison of Triglyceride (mg/dl)

Visits	Group I (n=270)			Group II (n=270)			Group III (n=270)			Statistical significance (ANOVA)*		Between Group comparison (Tukey HSD test 'p' value)		
	No.	Mean	SD	No.	Mean	SD	No.	Mean	SD	F	'p'	I vs II	I vs III	II vs III
Baseline	270	124.08	6.87	270	124.13	6.75	270	124.27	6.78	0.055	0.946	0.996	0.945	0.970
At 4 wks	246	135.57	7.58	251	137.88	7.42	257	140.32	7.64	24.922	0.000	0.02	0.000	0.01
At 8 wks	207	151.80	12.85	234	154.39	10.60	244	159.05	8.58	26.856	0.000	.031	0.000	0.000
At12wks	187	166.37	9.20	228	167.33	13.00	237	167.38	9.03	0.577	0.562	.628	.596	.999

Table 2(b): Within Group evaluation of Change among patients completing 12 weeks of treatment

Group	No. of patients completing 12 wks treatment	At Baseline		At 12 weeks		Statistical Significance (Paired 't'-test)	
		Mean	SD	Mean	SD	't'	'p'
I	187	123.91	6.83	166.37	9.20	-239.01	<0.001
II	228	123.66	6.79	167.33	13.00	-68.63	<0.001
III	237	124.10	6.68	167.38	9.03	-266.78	<0.001

Table 3(a): Inter and between group comparison of HDL (mg/dl)

Visits	Group I (n=270)			Group II (n=270)			Group III (n=270)			Statistical significance (ANOVA)*		Between Group comparison (Tukey HSD test 'p' value)		
	No.	Mean	SD	No.	Mean	SD	No.	Mean	SD	F	'p'	I vs II	I vs III	II vs III
Baseline	270	47.37	4.27	270	47.43	4.29	270	47.44	4.30	0.022	.979	.985	.980	1.000
At 4 wks	246	47.08	4.210	251	46.87	4.254	257	48.07	4.186	5.821	.003	.841	.025	.004
At 8 wks	207	47.47	4.272	234	47.23	4.317	244	48.69	4.221	8.090	.000	.816	.007	.001
At12wks	187	47.81	4.27	228	47.58	4.32	237	50.31	4.25	28.88	.000	.849	.000	.000

Table 3(b): Within Group evaluation of Change among patients completing 12 weeks of treatment

Group	No. of patients completing 12 wks treatment	At Baseline		At 12 weeks		Statistical Significance (Paired 't'-test)	
		Mean	SD	Mean	SD	't'	'p'
I	187	47.41	4.25	47.81	4.27	-15.30	<0.001
II	228	47.43	4.36	47.56	4.32	-6.89	<0.001
III	237	47.35	4.29	50.33	4.25	-86.39	<0.001

Table 4 (a): Inter and between group comparison of LDL (mg/dl)

Visits	Group I (n=270)			Group II (n=270)			Group III (n=270)			Statistical significance (ANOVA)*		Between Group comparison (Tukey HSD test 'p' value)		
	No.	Mean	SD	No.	Mean	SD	No.	Mean	SD	F	'p'	I vs II	I vs III	II vs III
Baseline	270	65.77	8.42	270	68.56	8.60	270	60.64	7.98	62.611	<0.001	.000	.000	.000
At 4 wks	246	79.31	9.200	251	81.90	9.259	257	68.95	8.261	150.357	.000	.04	.000	.000
At 8 wks	207	87.91	10.0	234	87.08	9.73	244	70.69	8.14	233.278	.000	.758	.000	.000
At12wks	187	88.51	10.06	228	87.52	10.06	237	70.24	8.725	258.270	.000	.551	.000	.000

Table 4(b) : Within Group evaluation of Change among patients completing 12 weeks of treatment

Group	No. of patients completing 12 wks treatment	At Baseline		At 12 weeks		Statistical Significance (Paired 't'-test)	
		Mean	SD	Mean	SD	't'	'p'
I	187	66.18	8.62	88.51	10.06	-150.84	<0.001
II	228	68.60	8.80	87.53	10.06	-99.12	<0.001
III	237	60.85	7.88	70.24	8.73	-95.98	<0.001

References:

1) Depression. NIMH. nimh.nih.gov. May 2016, Retrieved 31 July 2016.
2) Ustun TB, Ayuso-Mateos JL, Chatterji s, et al. Global burden of depressive disorders in the year 2000. British Journal of Psychiatry 2004; 184:386-92.
3) Thirunavukarasu M and Thirunavukarasu P. Training and National deficit of psychiatrists in India - A critical analysis. Indian J Psychiatry, 2010; 52:83.
4) Colin A, Reggers J, Castronovo V, et al. Lipids, depression and suicide. Encephale, 2003; 29:49-58.
5) Ghaemi SN, Shields GS, Hegarty JD, et al. Cholesterol levels in mood disorders: High or low? Bipolar Disord, 2000; 2:60 - 4.
6) Brunner J, Parhofer KG, Schwandt P, et al. Cholesterol, essential fatty acid and suicide. Pharmacopsychiatry. 2002; 35:15.
7) Takei N, Kunugi H and Nanko S. Low serum cholesterol and suicide attemps. Br J Psychiatry, 1994; 164: 702-3.
8) Papassotiropoulos A, Hawellek B, Frahnert C, et al. The risk of suicidality in psychiatric inpatients increase with low serum cholesterol, pharmacopsychiatry, 1999; 32: 1-4.
9) Gallerni M, Manfredini R and Caracciioli S. Serum cholesterol concentrations and parasuicide. BMJ, 1995; 310: 1632-6.
10) Agargum MY. Serum cholesterol concentration, depression and anxiety (editorial). Acta Psychiatr scand 2002; 105: 8183.
11) Borgherini G, Dorz S, Conforti D, et al. Serum cholesterol and psychological distress in hospitalized depressed patients. Acta Psychiatr Scand 2002; 105:149-52.
12) Manfredini R, Caracciolo S, Salmi R et al. The association of low serum cholesterol with depression and suicide behaviour; new hypotheses for the missing link. Journal of international medical research 2000; 28: 247-257.
13) Bucolo G and David H. Quantitative determination of serum triglycerides by the use of enzymes. Clin Chem. 1973; May; 19(5):476-82.
14) Divyashree M, Jayanthi CR and Chandrashekar H. A comparative study of efficacy and safety of conventional versus newer antidepressants in patients with depressive episode in a tertiary care hospital. Journal of Chemical and Pharmaceutical Research, 2014; 6(2):516-524.
15) Shahsavand Ananloo E, Ghaeli P, Kamkar MZ, et al. Comparing the effects of fluoxetine and imipramine on total cholesterol, triglyceride, and weight in patients with major depression. DARU Journal of Pharmaceutical Sciences, 2013; 21:4.
16) Murat Kesim, Ahmet Tiryaki, Mine Kadioglu et al. The effects of sertraline on blood lipids, glucose, insulin and HBA1C levels: A prospective clinical trial on depressive patients. J Res Med Sci, 2011(Dec); 16(12): 1525 - 1531.
17) Sansone RA. Cholesterol quandaries: Relationship to depression and the suicidal experience. Psychiatry (Edgmont), 2008; 5:22-34.
18) De Berardis D, Marini S, Piersanti M, et al. The Relationships between Cholesterol and Suicide: An Update. ISRN Psychiatry, 2012; 2012: 1-6.
19) Papakostas GI, Ongür D, Iosifescu DV, et al. Cholesterol in mood and anxiety disorders: Review of the literature and new hypotheses. Eur Neuropsychopharmacol, 2004; 14:135 - 42.
20) Steegmans PH, Fekkes D, Hoes AW, et al. Low serum cholesterol concentration and serotonin metabolism in men. BMJ, 1996; 312:221.
21) Hawton K, Cowen P. and Owens D. Low serum cholesterol and suicide. British Journal of Psychiatry, 1993; 162: 818-825.
22) Penttinen J. Hypothesis: lower serum cholesterol, suicide and interleukin-2. American Journal of Epidemiology, 1995; 141:716-718.
23) Terao T, Yoshimura R, Ohmori O, et al. Effect of serum cholesterol levels on metachlorophenylpiperazine- evoked neuroendocrine responses in healthy subjects. Biol Psychiatry, 1997; 41:974 - 8.
24) Maes M, Smith R, Christophe A, et al. Lower serum high-density lipoprotein cholesterol (HDL-C) in major depression and in depressed men with serious suicidal attempts: Relationship with immune-inflamatory markers. Acta Psychiatr Scand, 1997; 95:212-21.
25) Shibata H, Kumagai S, Watanabe S, et al. Relationship of serum cholesterols and vitamin E to depressive status in the elderly. J Epidemiol, 1999; 9:261-7.
26) Olusi SO and Fido AA. Serum lipid concentrations in patients with major depressive disorder. Biol Psychiatry, 1996; 40:1128-31.
27) Chang SS, Wen CP, Tsai MK, et al. Adiposity, its related biologic risk factors, and suicide: A cohort study of 542, 088 Taiwanese adults. Am J Epidemiol, 2012; 175: 804 - 15.
28) Partonen T, Haukka J, Virtamo J, et al. Association of low serum total cholesterol with major depression and suicide. Br J Psychiatry, 1999; 175:259-62.
29) Rafter D. Biochemical markers of anxiety and depression. Psychiatry Res, 2001;

103:93-6.
30) Troisi A. Low cholesterol is a risk factor for attentional impulsivity in patients with mood symptoms. Psychiatry Res, 2011; 188:83-7.
31) Sevincok L, Buyukozturk A and Dereboy F. Serum lipid concentrations in patients with comorbid generalized anxiety disorder and major depressive disorder. Can J Psychiatry 2001; 46:68-71.
32) Ledochowski M, Murr C, Sperner-Unterweger B, et al. Association between increased serum cholesterol and signs of depressive mood. Clin Chem Lab Med, 2003;41: 821-4.
33) Gabriel A. Changes in plasma cholesterol in mood disorder patients: Does treatment make a difference? J Affect Disord, 2007; 99:273-8.
34) Roessner V, Demling J and Bleich S. Doxepin increases serum cholesterol levels. Can J Psychiatry, 2004; 49:74-5.
35) Yeragani VK, Pohl R, Balon R, et al. Increased serum total cholesterol to HDL-Cholesterol ratio after imipramine. Psychiatry Res, 1990; 32:207-9.
36) Lara N, Baker GB, Archer SL, et al. Increased cholesterol levels during paroxetine administration in healthy men. J Clin Psychiatry, 2003; 64:1455-9.
37) Kurt E, Guler O, Serteser M, et al. The effects of electroconvulsive therapy on ghrelin, leptin and cholesterol levels in patients with mood disorders. Neurosci Lett, 2007; 426:49-53.
38) Perry PJ, Garvey MJ, Dunner DL, et al. A report of trazodone-associated laboratory abnormalities. Ther Drug Monit, 1990;12:517-9.
39) Othmer E, Othmer SC, Stern WC, et al. Long-term efficacy and safety of bupropion. J Clin Psychiatry, 1983; 44:153-6.
40) Paykel ES, Mueller PS and De la Vergne PM. Amitriptyline, weight gain and carbohydrate craving: a side effect. Br J Psychiatry, 1973; 123:501-507.
41) Berken GH, Weinstein DO and Stern WC: Weight gain: A side-effect of tricyclic antidepressants. J Affect Disord 1984, 7:133 - 138.
42) Garland EJ, Remick RA and Zis AP: Weight gain with antidepressants and Raeder lithium. J Clin Psychopharmacol, 1988; 8: 323 - 330.
43) Raeder MB, Bjelland I, Emil Vollset S, et al. Obesity, dyslipidemia, and diabetes with selective serotonin reuptake inhibitors: the Hordaland health Study. J Clin Psychiatry, 2006; 67:1974 - 1982.
44) Raeder MB, Ferno J, Glambek M, et al. Antidepressant drugs activate SREBP and up-regulate cholesterol and fatty acid biosynthesis in human glial cells. Neurosci Lett, 2006; 395:185 - 190.
45) Lautt WW, Ming Z and Legare DJ. Attenuation of age and sucrose induced insulin resistance and syndrome X by a synergistic antioxidant cocktail: the AMIS syndrome and HISS hypothesis. Can J Physiol Pharmacol, 2010; 88(3):313 - 23.
46) Patarrao RS, Lautt WW, Afonso RA, et al. Mealinduced insulin sensitization and its parasympathetic regulation in humans. Can J Physiol Pharmacol, 2008; 86(12):880 - 8.
47) Sadri P, Reid MA, Afonso RA, et al. Mealinduced Insulin sensitization in conscious and anaesthetized rat models comparing liquid mixed meal with glucose and sucrose. Br J Nutr, 2006; 95(2):288 - 95.